# TISSUE CHARACTERIZATION BASED ON IMPEDANCE IMAGES AND ON IMPEDANCE MEASUREMENTS

## CROSS REFERENCE TO RELATED APPLICATION

This application is a Continuation-in-Part of International Application No. PCT/US95/06141, filed May 19, 1995, the disclosure of which is incorporated by reference in its entirety.

## FIELD OF THE INVENTION

The present invention relates to systems for tissue characterization based on impedance measurement at a point or at an array of points.

## BACKGROUND OF THE INVENTION

The measurement of electrical potentials on the skin has many uses. For example, electrocardiograms are derived from measuring the potential generated by the heart of a patient at various points on the skin.

Skin potentials are also measured in apparatus for determining the electrical impedance of human tissue, including two-dimensional (e.g., U.S. Patents 5,063,937, 4,291,708 and 4,458,694) or three-dimensional (e.g., U.S. Patents 4,617,939 and 4,539,640) mapping of the tissue impedance of the body. In such systems an electrical potential is introduced at a point or points on the body and measured at other points at the body. Based on these measurements and on algorithms which have been developed over the past several decades, an impedance map or other indication of variations in impedance can be generated.

U.S. Patents 4,291,708 and 4,458,694 and "Breast Cancer screening by impedance measurements" by G. Piperno et al. Frontiers Med. Biol. Eng., Vol. 2, pp 111-117, the disclosures of which are incorporated herein by reference, describe systems in which the impedance between a point on the surface of the skin and some reference point on the body of a patient is determined. These references describe the use of a multi-element probe for the detection of cancer, especially breast cancer, utilizing detected variations of impedance in the breast.

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In these references a multi-element probe is described in which a series of flat, stainless steel, sensing elements are mounted onto a PVC base. A lead wire is connected between each of these elements and detector circuitry. Based on the impedance measured between the elements and a remote part of the body, signal processing circuitry determines the impedance variations in the breast. Based on the impedance

1  determination, tumors, and specially malignant tumors, can
2  be detected.
3      The multi- lement probe is a critical component in this
4  system and in other systems which use such probes. On one
5  hand the individual elements must make good contact with th
6  skin and with the corresponding points on the sensing or
7  processing electronics while also being well isolated from
8  each other. On the other hand, use of gels to improve skin
9  contact carries the risk of cross-talk, dried gel build-up on
10 the elements and inter-patient hygienic concerns.
11     A paper titled "Capacitive Sensors for In-Vivo
12 Measurements of the Dielectric Properties of Biological
13 materials" by Karunayake P.A.P. Esselle and Stanislaw S.
14 Stuchly (IEEE Trans. Inst & Meas. Vol. 37, No. 1, p. 101-105)
15 describes a single element probe for the measurement of in
16 vivo and in vitro measurements of the dielectric properties
17 of biological substances at radio and microwave frequencies.
18 The sensor which is described is not suitable for impedance
19 imaging.
20     A paper entitled "Messung der elektrischen Impedance von
21 Organen- Apparative Ausrüstung für Forschung und klinishe
22 Anwendung" by E. Gersing (Biomed. Technik 36 (1991), 6-11)
23 describes a system which uses single element impedance probes
24 for the measurement of the impedance of an organ. The device
25 described is not suitable for impedance imaging.
26     A Paper titled "MESURE DE L'IMPEDANCE DES TISSUS
27 HEPATIQUELES TRANSFORMES PAS DES PROCESSUS LESIONELS" by J.
28 Vrana et al. (Ann. Gastroentreol. Hepetol., 1992, 28, no. 4,
29 165-168) describes a probe for assessing deep tissue by use
30 of a thin injection electrode. The electrode was positioned
31 by ultrasound and specimens were taken for cytological and
32 histological assessment. The electrode was constituted on a
33 biopsy needle used to take the samples.
34     A paper titled "Continuous impedance monitoring during
35 CT-guided stereotactic surgery: relative value in cystic and
36 solid lesions" by V. Rajshekhar (British Journal of
37 Neurosurgery (1992) 6, 439-444) describes using an impedance
38 probe having a single electrode to measure the impedance
39 characteristics of lesions. The objective of the study was to

1 use the measurements made in the lesions to determine the
2 extent of th lesions and to localize th lesions more
3 accurately. Th probe is guided to the tumor by CT and f ur
4 measurements were made within the lesion as the probe passed
5 through the lesion. A biopsy of the lesion was performed
6 using the outer sheath of the probe as a guide to position,
7 after the probe itself was withdrawn.

8 A paper titled "Rigid and Flexible Thin-Film Multi-
9 electrode Arrays for Transmural Cardiac Recording" by J. J.
10 Mastrototaro et al. (IEEE TRANS. BIOMED. ENG. Vol. 39, No. 3,
11 March 1992, 271-279) describes a needle probe and a flat
12 probe each having a plurality of electrodes for the
13 measurement of electrical signals generated in the heart.

14 A paper entitled "Image-Based Display of Activation
15 Patterns Derived from Scattered Electrodes" by D. S. Buckles
16 et al. (IEEE TRANS. BIOMED ENGR. Vol. 42, No. 1, January
17 1995, 111-115) describes a system for measurement of
18 electrical signals generated on the heart by use of an array
19 of electrodes on a substrate. The heart with the electrodes
20 in place is viewed by a TV camera and an operator marks the
21 positions of the electrodes on a display. The system then
22 displays the heart (as visualized prior to the placement of
23 the electrodes) with the position markings.

24 A paper entitled "Development of a Multiple Thin-Film
25 Semimicro DC-Probe for Intracerebral Recordings" by G. A.
26 Urban et al. (IEEE TRANS. BIOMED ENGR. Vol. 37, No. 10,
27 October 1990, 913-917) describes an elongate alumina ceramic
28 probe having a series of electrodes along its length and
29 circumference for measuring functional parameters (electrical
30 signals) in the brain. Electrophysiological recording,
31 together with electrostimulation at the target point during
32 stereotactic surgery, was performed in order to ensure exact
33 positioning of the probe after stereotactic calculation of
34 the target point. Bidimensional X-Ray imaging was used in
35 order to verify the exact positioning of the electrode tip.

## SUMMARY OF THE INVENTION

36 It is an object of certain aspects of the invention to
37 provide a multi-element probe having improved and more
38 provide a multi-element probe having improved and more
39 uniform and repeatable contact with the skin with minimal

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1 operator exp rtise and minimal risk of cross-patient
2 contamination.
3     It is an object of c rtain aspects of the invention to
4 provide improved inter-element electrical isolation, and to
5 permit sliding of the probe while it is urged against the
6 skin.
7     It is an object of certain aspects of the invention to
8 provide a relatively inexpensive disposable multi-element
9 probe.
10     It is an object of certain aspects of the invention to
11 provide a multi-element probe having sufficient transparency
12 to allow for viewing of tissue surface features and to allow
13 for referencing the probe with respect to physical features
14 of or on the skin.
15     It is an object of certain aspects of the invention to
16 provide a method of distinguishing between artifacts and
17 abnormalities.
18     It is an object of certain aspects of the invention to
19 provide a system for electrical impedance imaging which
20 simultaneously acquires, uses and preferably displays both
21 capacitance and conductance information.
22     It is an object of certain aspects of the invention to
23 provide a system for electrical impedance testing of the
24 breast or other body region which provides more accurate
25 information regarding the position of impedance abnormalities
26 detected in the breast or other region.
27     It is an object of certain aspects of the invention to
28 provide for electrical impedance testing with a variable
29 spatial resolution.
30     It is an object of certain aspects of the invention to
31 provide for two dimensional electrical impedance testing
32 giving an indication of the distance of an abnormality from
33 the surface of the skin.
34     It is an object of certain aspects of the invention to
35 provide apparatus especially suitable for breast impedance
36 measurements.
37     It is an object of certain aspects of the invention to
38 provide guidance for placement of elongate objects such as
39 biopsy needles, localization needles, fiber optic endoscopes

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1 and the lik using real time and/or recorded st reotactic
2 images to guid the object.
3 It is a further obj ct of c rtain asp cts of the
4 invention to provid a biopsy needle having an impedance
5 measuring function to aid in the taking of a biopsy.
6 It is an object of certain aspects of the invention to
7 provide more direct comparison between the results of
8 electrical impedance maps and the results of optical,
9 ultrasound or other imaging modalities.
10 It is an object of certain aspects of the invention to
11 provide apparatus and method for indicating, on an anatomical
12 illustration, the location and region from which an impedance
13 image, shown together with the illustration is derived.
14 It is an object of certain aspects of the invention to
15 provide apparatus which facilitates direct comparison between
16 X-Ray and impedance mammographic images, as for example by
17 superposition of the images.
18 It is an object of certain aspects of the invention to
19 provide a method of determining a polychromic (multi-
20 frequency) impedance map.
21 It is an object of certain aspects of the invention to
22 optimize the impedance mapping utilizing a pulsed voltage
23 excitation.
24 It is an object of certain aspects of the invention to
25 provide palpation and tactile sensing of an area while
26 simultaneously providing an impedance image of the area.
27 It is an object of certain aspects of the invention to
28 allow for the identification of tissue types from impedance
29 maps.
30 In general, the term "skin" as used herein means the
31 skin or other tissue of a subject.
32 The present inventor has found that when, in an
33 impedance image, an anomaly is perceived, the type of tissue
34 underlying the position of the anomaly on the image may
35 generally be determined by a characterization procedure which
36 includes the determination of a number of polychromic
37 measures for the anomaly and surrounding non-anomalous tissue
38 and comparison of the measures with ranges of values of
39 individual polychromic measures or their combinations which

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1  are characteristic of various types of tissue. It has been
2  found that normal tissue such as br ast tissue, nipples and
3  the infra-mammary ridg , ribs and Costo-chondral Junctions
4  and benign hyperplasia can generally b  distinguished from
5  cancerous tumors and precancerous atypical hyperplasia. These
6  measures are based on the structure and form of the deviation
7  of the capacitance and conductance of the anomalous portion
8  of the image from that of the surrounding, normal tissue. For
9  those cases where there is some ambiguity between some types
10  of tissue, knowledge of the anatomy of the imaged area or
11  palpation of the area can often remove the ambiguity or
12  additional views can be taken to remove the ambiguity.
13     In an image the measures are preferably determined by
14  comparing the capacitance or conductance of the anomalous
15  pixels on the image to be characterized with the capacitance
16  or conductance of normative tissue around the mean or median
17  value of the capacitance or conductance, typically in terms
18  of quantified deviation of a given pixel or region from the
19  median in the image, as measured in multiples of the
20  estimated standard deviation or coefficient of variance.
21     The method is also potentially useful to determine
22  tissue types in situations where either a single impedance
23  probe is used or where the image is small and only anomalous
24  areas are imaged. In these cases the comparison is made
25  between the values of capacitance or conductance measured for
26  the anomalous region as compared to the capacitance or
27  conductance measured for a nearby region known to be normal.
28     As used herein the term immitance means either the
29  complex admittance or impedance. Furthermore the term
30  polychromic measure is a measure which is based on the
31  immitance or on the real or imaginary part thereof or on a
32  combination of the immitance and/or the real part thereof
33  and/or the imaginary part thereof at a plurality of
34  frequencies, i.e., on the spectrum thereof.
35     There is therefore provided, in accordance with a
36  preferred embodiment of the invention apparatus for aiding in
37  the identification of tissue type for an anomalous tissue in
38  an impedance image comprising:
39     means for providing an polychromic immitance map of a

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1 portion of the body;
2     means for determining a plurality of polychromic
3 measures, preferably normalized m asures, of an anomalous
4 region of the immitance image; and
5     a display which displays an indication based on said
6 plurality of polychromic measures.
7     Preferably the apparatus includes means for providing a
8 map of said polychromic measures and wherein said indication
9 includes a display of a plurality of said maps.
10     In a preferred embodiment of the invention the display
11 includes an overlay of maps of said polychromic measures.
12     Preferably the apparatus includes means for matching the
13 values of the plurality of measures with predetermined values
14 of the measures to identify the tissue type of the anomalous
15 tissue.
16     In one preferred embodiment of the invention the
17 indication is the display of a map of said determined tissue
18 type.
19     There is further provided, in accordance with a
20 preferred embodiment of the invention, apparatus for
21 determining a tissue type for an anomalous tissue comprising:
22     means for determining a plurality of polychromic
23 measures of the anomalous tissue; and
24     means for matching the values of the plurality of
25 measures with predetermined values of the measures to
26 identify the tissue type of the anomalous tissue.
27     There is further provided, in accordance with a
28 preferred embodiment of the invention, a method of
29 determining a tissue type for tissue in an anomalous region
30 in an immitance image, comprising:
31     determining a plurality of polychromic measures,
32 preferably normalized measures, of said anomalous region; and
33     matching the values of the plurality of measures to
34 identify the tissue type of the anomalous region.
35     There is further provided, in accordance with a
36 preferred embodiment of the invention, a method of
37 determining a tissue type for an anomalous tissue:
38     determining a plurality of polychromic measures,
39 preferably normalized measures, of the anomalous tissue;

matching the valu s of th plurality of measures with
pr determined values to identify the tissue type of the
anomalous tissu .

Preferably, one of the polychromic measures is derived
from the sum, over a plurality of frequencies, of the
positive deviations of the capacitance of the anomaly from
that of typical nonanomolous regions.

Preferably, one of the polychromic measures is derived
from the sum, over a plurality of frequencies, of the
negative deviations of the capacitance of the anomaly from
that of typical nonanomolous regions.

Preferably, one of the polychromic measures is derived
from the sum, over a plurality of frequencies, of the
positive deviations of the conductance of the anomaly from
that of typical nonanomolous regions.

Preferably one of the measures is the integral of the
phase or the sum of phase values over a range of frequencies.

Preferably, one of the measures is the difference
between the integral of the difference between the phase at a
point and the mean or median value of the phase in the image,
over a range of frequencies.

Preferably, one of the measures is the derivative of the
capacitance curve or its logarithm as a function of
frequency, evaluated at a given frequency.

Preferably, one of the measures is the derivative of the
conductance curve or its logarithm as a function of
frequency, evaluated at a given frequency.

Preferably, one of the measures is a frequency at which
the phase of the impedance reaches a specified value,
preferably 45 degrees.

## BRIEF DESCRIPTION OF THE DRAWINGS

1  Th  inv ntion will be more fully understood and
2  appreciated from th  following detailed description, taken in
3  conjunction with the drawings in which:
4      Fig. 1 is an overall view of an imp dance mapping system
5  especially suitable for breast impedance mapping in
6  accordance with a preferred embodiment of the invention;
7      Fig. 2 is a perspective view of an imaging head suitable
8  for breast impedance mapping in accordance with a preferred
9  embodiment of the invention;
10     Figs. 3A and 3B show partially expanded views of two
11  preferred probe head configurations suitable for use in the
12  imaging head of Fig. 2;
13     Fig. 4 is a top view of a portion of a multi-element
14  probe in accordance with a preferred embodiment of the
15  invention;
16     Fig. 5A is a partial, partially expanded cross-
17  sectional side view of the probe of Fig. 4 along lines V-V,
18  suitable for the probe head configuration of Fig. 3B;
19     Fig. 5B is a partially expanded cross-sectional side
20  view of an alternative probe in accordance with a preferred
21  embodiment of the invention;
22     Fig. 5C shows an alternative embodiment of a multi-
23  element probe, in accordance with a preferred embodiment of
24  the invention;
25     Fig. 6A is a perspective view of a hand held probe in
26  accordance with a preferred embodiment of the invention;
27     Fig. 6B shows a partially expanded bottom view of the
28  probe of Fig. 6A, in accordance with a preferred embodiment
29  of the invention;
30     Fig. 7A is a perspective view of a fingertip probe in
31  accordance with a preferred embodiment of the invention;
32     Fig. 7B shows a conformal multi-element probe;
33     Fig. 8 shows an intra-operative probe used determining
34  the position of an abnormality in accordance with a preferred
35  embodiment of the invention;
36     Fig. 9 shows a laparoscopic probe in accordance with a
37  preferred embodiment of the invention;
38     Fig. 10 shows a biopsy needle in accordance with a
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1  preferred embodiment of the invention;
2      Fig. 11A illustrat s a m thod of using the biopsy needle
3  of Fig. 10, in accordance with a preferred embodiment of the
4  inv ntion;
5      Fig. 11B illustrates a portion of a display used in
6  conjunction with the method of Fig. 11A;
7      Fig. 11C shows a biopsy guiding system in accordance
8  with a preferred embodiment of the invention;
9      Fig. 11D shows a frontal biopsy guiding system in
10  accordance with a preferred embodiment of the invention;
11      Fig. 11E shows a lateral biopsy guiding system in
12  accordance with a preferred embodiment of the invention;
13      Fig. 12 shows, very schematically, the inter-operative
14  probe of Fig. 8 combined with a video camera use to more
15  effectively correlate an impedance measurement with placement
16  of the probe.
17      Fig. 13 illustrates a laparoscopic probe according to
18  the invention used in conjunction with a  fiber-optic
19  illuminator-imager;
20      Fig. 14 illustrates a display, according to a preferred
21  embodiment of the invention showing both capacitive and
22  conductance images illustrative of atypical hyperplasia;
23      Fig. 15 illustrates a display, according to a preferred
24  embodiment of the invention showing both capacitive and
25  conductance images illustrative of a carcinoma;
26      Fig. 16 illustrates a method useful for verifying a
27  detected local impedance deviation as being non-artifactal
28  and for estimating the deviation;
29      Figs. 17A and 17B are a block diagram of circuitry
30  suitable for impedance mapping in accordance with a preferred
31  embodiment of the invention; and
32      Figs. 18A-18C show maps of polychromic measures
33  characteristic of certain tissue types.

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# DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

1    Reference is made to Figs. 1 and 2 which illustrate an

2  imp danc mapping device 10 suitable for mapping the

3  impedance of a breast.

4    Mapping device 10 includes an imaging head 12, which is

5  described below, which holds the breast and provides contact

6  therewith for providing electrical excitation signals thereto

7  and for receiving resultant electrical signals therefrom.

8  Signals to and from the head are generated and received by a

9  computer/controller 14 which produces impedance maps of the

10  breast under test for display on a monitor 16. The impedance

11  maps may be stored in computer/controller 14 for later

12  viewing or processing or hard copies may be provided by a

13  hard copy device 18 which may be a laser printer, video

14  printer, Polaroid or film imager or multi-imager.

15    The entire mapping device 10 may be conveniently mounted

16  on a dolly 20 to facilitate placement of the imaging head

17  with respect to the patient.

18    Fig. 1 also shows a hand held probe 100, described in

19  more detail below, and a reference probe 13.

20    Fig. 2 shows imaging head 12 in more detail. Head 12

21  comprises a movable lower plate probe 22 and a stationary

22  upper plate probe 24 which is mounted on a pair of rails 26

23  to allow the distance between plate probes 22 and 24 to be

24  varied.

25    Movement of plate probe 22 along rails 26 may be

26  achieved either by a motor (not shown) including suitable

27  protection against over-pressure as is traditional in X-ray

28  breast imaging, or by hand.

29    Either or both of plate probes 22 and 24 are provided

30  with multi-element probes 28 and 30 respectively, which are

31  described more fully below, which electrically contact the

32  breast with a plurality of sensing elements to optionally

33  provide electrical excitation to the breast and to measure

34  signals generated in response to the provided signals.

35  Alternatively, electrical excitation to the breast is

36  provided by reference probe 13 which is placed on the arm,

37  shoulder or back of the patient, or other portion of the

38  patient.

1     In practice, a breast is inserted between probes 28 and
2 30 and plate probe 24 is lowered to compress th breast
3 betw en the probes. This compression reduc s the distance
4 between the probes and provides better contact b tween the
5 sensing elements and the skin of the br ast. Although
6 compression of the breast is desirable, the degree of
7 compression required for impedance imaging is much lower than
8 for X-Ray mammography, and the mapping technique of the
9 present invention is typically not painful.
10     Alternatively or additionally, the probes are curved to
11 conform with the surface of the breast.
12     Head 12 is provided with a a pivot (not shown) to allow
13 for arbitrary rotation of the head about one or more of its
14 axes. This allows for both medio-lateral and cranio-caudal
15 maps of the breast to be acquired, at any angular orientation
16 about the breast. Preferably, head 12 may be tilted so that
17 the surfaces of plate probes 22 and 24 are oriented with a
18 substantial vertical component so that gravity assists the
19 entry of the breast into the space between the maximum extent
20 and to keep it from inadvertently falling out. This is
21 especially useful when the patient leans over the plates so
22 that her breasts are positioned downwardly between the plate
23 probes.
24     Furthermore, in a preferred embodiment of the invention,
25 one or both of probes 28 and 30 may be rotated about an axis
26 at one end thereof, by a rotation mechanism 27 on their
27 associated plate probes 22 or 24, such as is shown in Fig. 2
28 for probe 28. Additionally or alternatively, probes 28 and/or
29 30 may be slidable, as for example along members 31.
30     Such additional sliding and rotating flexibility is
31 useful for providing more intimate skin contact of the probes
32 with the breast, which has a generally conical shape.
33 Furthermore, such flexibility allows for better imaging of
34 the areas of the breast near the chest wall or the rib cage,
35 which are extremely difficult to image in x-ray mammography.
36     Figs. 3A and 3B show partially expanded views of two
37 probe head configurations suitable for use in the imaging
38 head of Fig. 2, in accordance with preferred embodiments of
39 the invention.

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1    In the embodiment of Fig. 3A, a preferably removable
2 multi-element probe 62, which is described below in more
3 detail, is attached to a probe head base 50 via a pair of
4 mating multi-pin connectors 51 and 52. A cable 53 couples
5 connector 52 to computer 14. When multi-element probe 62 is
6 inserted into base 50 (that is to say, when connector 51 is
7 fully inserted into connector 52), the relatively stiff
8 bottom of probe 62 rests on ledges 54 formed in the base,
9 such that the surface 55 of the base and the surface of
10 element 62 are preferably substantially coplanar.
11    In the embodiment of Fig. 3B, a series of contacts 82
12 are formed on base 50 and a disposable multi-element probe
13 62' is attached to the contacts as described below with
14 reference to Fig. 5A and 5B. Cable 53 couples the contacts to
15 computer 14.
16    Figs. 4, 5A and 5B show top and side views of a portion
17 of multi-element probe 62' and contacts 74, while Figs. 5A
18 and 5B show a partially expanded cross-sectional side view
19 of probe 62' along lines V-V. While the embodiment shown in
20 Figs. 4, 5A and 5B is especially suitable for the probe head
21 configuration of Fig. 3B, much of the structure shown in
22 these figures 5 is common to multi-element probes used in
23 other configurations described herein.
24    As shown in Figs. 4, 5A and 5B, disposable multi-element
25 probe 62' preferably incorporates a plurality of sensing
26 elements 64, separated by separator or divider elements 66.
27    As shown more clearly in Figs. 5A and 5B, sensing
28 elements 64, comprise a bio-compatible conductive material
29 (for example Neptrode E0751 or Neptrode E0962 Hydrogel
30 distributed by Cambrex Hydrogels, Harriman, NY) such as is
31 sometimes used for ECG probes in a well 70 formed by a first,
32 front, side of a mylar or other flexible, non-conducting
33 substrate 68, such as a thin mylar sheet and the divider
34 elements 66. A suitable thickness for the mylar sheet is
35 approximately 0.2 mm for probe 62'. The substrate is
36 preferably pierced in the center of each well. The hole
37 resulting from the piercing is filled with a conducting
38 material which is also present on the bottom of well 70 and
39 on a second, back, side of substrate 68 to form a pair of

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1   electrical contacts 72 and 74 on either side of the
2   substrate and an electrically conducting feed-through 76
3   between th pair of contacts. As shown, a separate contact
4   p ir and feed-through is provided for each sensing element.
5       Alternatively, the substrate may be form d of any
6   suitable inert material including plastics such as
7   polyethylene, polypropylene, PVC, etc.
8       Wells 70 may be formed in a number of ways. One method
9   of forming the wells is to punch an array of square holes in
10  a sheet of plastic, such as polypropylene, which is about
11  0.2-1mm thick. This results in a sheet containing only the
12  divider elements. This sheet is bonded to substrate 68 which
13  has been pre-pierced and in which the contacts and feed-
14  throughs have been formed. Another method of forming the
15  wells is to emboss a substrate containing the contacts and
16  feed-throughs to form divider elements in the form of ridges
17  which protrude from the substrate as shown in Fig. 5B. Yet
18  another method of producing the wells is by printing the well
19  walls using latex based ink or other bio-compatible material
20  having a suitable firmness and flexibility. Another method of
21  production is by injection molding of the substrate together
22  with the divider elements. And yet another method of
23  producing the wells is by laminating to the substrate a
24  preformed grid made by die cutting the array of divider
25  elements in a sheet of plastic, injection molding, or other
26  means.
27      The conductors and feed-throughs may be of any
28  conductive material which will provide reliable feed-through
29  plating of the holes. One method of manufacturing the
30  contacts and holes is by screen printing of the contacts on
31  both sides of the substrate. If conductive paste having a
32  suitable viscosity is used, the paste will fill the hole and
33  form a reliable contact between contacts 72 and 74. Although
34  many conductive materials can be used, non-polarizing
35  conductors, such as silver/silver chloride are preferred. A
36  conductive paste suitable for silk screening the conductors
37  onto the substrate is Pad Printable Electrically conductive
38  Ink No. 113-37 manufactured and sold by Creative Materials
39  Inc., Tyngsboro, MA.        - 14 -

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1      In general contacts 72 and 74 are only 10-200 microns
2 thick and wells 70 are generally filled with conductive
3 viscous gel material or hydrogel material to within about
4 0.2 mm of the top of the dividing elements. In g neral, if
5 low separators are used, the hydrogel may be omitted.
6 However, in the preferred embodiment of the invention, the
7 wells are at least partially filled by hydrogel or a similar
8 material.

9      Hydrogel is available in both UV cured and heat cured
10 compositions. In either case a measured amount of uncured
11 semi-liquid hydrogel is introduced into each well and the
12 hydrogel is cured. Alternatively, the wells are filled with
13 the uncured material and a squeegee which is pressed against
14 the top of the divider elements with a predetermined force is
15 moved across the top of the divider elements. This will
16 result in the desired gap between the top of the hydrogel and
17 the top of the wells.

18      In an alternative embodiment of the invention, the
19 hydrogel material is replaced by a sponge material or similar
20 supportive matrix impregnated with conductive viscous gel or
21 the well is simply filled with the conductive gel to the
22 desired height.

23      During use of the probe, the probe is urged against the
24 skin which is forced into the wells and contacts the hydrogel
25 or alternative conductive material. Optionally, a somewhat
26 viscous conductive gel, such as Lectron II Conductivity Gel
27 (Pharmaceutical Innovations, Inc. Newark, NJ), may be used to
28 improve contact with the skin. In this case, the dividing
29 elements will reduce the conduction between the cells such
30 that the substantial independence of the individual
31 measurements is maintained. Alternatively, the conductive gel
32 may be packaged together with the probe, with the conductive
33 gel filling the space between the top of the hydrogel and the
34 top of the wells. The use of a conductive gel is preferred
35 since this allows for sliding movement of the probe and its
36 easy positioning while it is urged against the skin. The
37 separators substantially prevent the conductive gel from
38 creating a low conductance path between adjoining sensing
39 elements and also keep the hydrogel elements from touching

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1 each other when the probe is applied to the skin with some

2 pressure.

3     ·In a further preferred embodiment of the invention, the

4 sensing el m nts are formed of a conductive foam or sponge

5 material such as silicone rubber or other conductive rubber

6 or other elastomer impregnated with silver or other

7 conductive material, as shown in Fig. 5C. Fig. 5C shows the

8 sensing elements without walls 66. Elements which protrude

9 from the substrate as shown in Fig. 5C may achieve

10 substantial electrical isolation from one another by spacing

11 them far enough apart so that do not contact each other in

12 use or by coating their lateral surfaces with insulating

13 material such as polyethylene or other soft non-conductive

14 plastic or rubber.

15     For relatively short rigid or compressible elements, it

16 has been found that reducing the size of the sensing elements

17 such that no more than 70% (and preferably no more than 50%)

18 of the area of the array is covered is sufficient to reduce

19 the "cross-talk" between adjoining elements to an acceptable

20 level.

21     If sufficiently good isolation is achieved between probe

22 elements by their spacing alone, then foam or other elements

23 without hydrogel and without walls 66 may be provided.

24 Sensing elements such as those shown in Fig. 5C conform and

25 mate to uneven surfaces when pressed against tissue.

26     Multi-element probe 62', which is preferably used for

27 only one patient and then discarded, is preferably removably

28 attached to a probe holder which preferably comprises a

29 printed circuit board 80 having a plurality of contacts 82

30 corresponding to the contacts 74 on the back of the

31 substrate, each PC board contact 82 being electrically

32 connected to a corresponding contact 74 on the substrate. To

33 facilitate alignment of the matching contacts, an alignment

34 guide 90 is preferably provided on or adjacent to PC board 80

35 (Fig. 4). This guide may consist of a series of guide marks

36 or may consist of a raised edge forming a well into or onto

37 which the substrate is inserted. Conductors within PC board

38 80 connect each of the contacts to one of the pins of

39 connector 51, which is preferably mounted on PC board 80.

1      Alternatively and preferably, as described below with
2 respect to Fig. 6B, the guide may consist of two or more pins
3 located on or near PC board 80, which fit into matching holes
4 in probe 62'.

5      Alternatively as shown in Fig. 5B, the back side of the
6 embossing of substrate 68 is used as the guide for one or
7 more protruding elements 83 which are preferably mounted on
8 PC board 80. Preferably a plurality of protruding elements
9 are provided to give good alignment of the substrate with the
10 PC board. The elements may run along the periphery of the
11 probe and form a frame-like structure as shown in Fig. 5B or
12 may run between the elements or may take the form of x shaped
13 protuberances which match the shape of the embossing at the
14 corners of the wells.

15      Protruding elements 83 may be formed of polycarbonate,
16 acetate, PVC or other common inert plastic, or of a
17 noncorrosive metal such as stainless steel.

18      A wire 84 is connected to each PC contact 82 and is also
19 connected to apparatus which provides voltages to and/or
20 measures voltages and/or impedances at the individual sensing
21 elements 64, as described below.

22      In a preferred embodiment of the invention, conductive
23 adhesive spots 86 preferably printed onto the back of the
24 substrate are used to electrically and mechanically connect
25 contacts 74 with their respective contacts 82. Preferably a
26 conductive adhesive such as Pressure Sensitive Conductive
27 Adhesive Model 102-32 (Creative Materials Inc.) is used.
28 Alternatively, the adhesive used for printing the
29 contacts/feed-throughs is a conducting adhesive and adhesive
30 spots 86 may be omitted. Alternatively, pins, which protrude
31 from the surface of PC board 80 and are connected to wires 84
32 pierce the substrate (which may be pre-bored) and contact the
33 gel or hydrogel in the wells. A pin extending from the
34 substrate may also be inserted into a matching socket in the
35 PC board to form the electrical connection between the
36 sensing element and the PC board. Alternatively, the entire
37 back side of the substrate can be adhered to the printed
38 circuit board surface using an anisotropically conductive
39 thin film adhesive which has a high conductivity between

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1  contacts 74 and 82 and which has a low conductivity resulting
2  in preferably many times higher resistance between adjoining
3  contacts than between matching contacts, in practic at least
4  one hundr d times different. An example of such adhesive is
5  tape NO. 3707 by MMM Corporation, Minneapolis MN. However,
6  due to the difficulty of applying such material without
7  trapped air bubbles, it may be preferably to apply adhesive
8  only to the contacts themselves. In practice a release liner
9  of polyethylene, mylar or paper with a non-stick surface on
10  one side is provided on the lower side of the adhesive sheet.
11  This liner protects the adhesive layer prior to connection of
12  the disposable multi-element probe to the probe holder and is
13  removed prior to the connection of the probe to the holder.
14      Preferably, the impedance between contacts 82 and skin
15  side of the conducting material in the wells should be less
16  than 100 ohms at 1 kHz and less than 400 ohms at 10 Hz.
17      Impedance between any pair of contacts 82, with the
18  multi-element probe mounted should preferably be greater than
19  10 kohm at 1 kHz or 100 kohm at 10 Hz.
20      Another suitable material for producing substrates is
21  TYVEX (DuPont) substrate which is made from a tough woven
22  polyolefin material available in various thicknesses and
23  porosities. If such material having a suitable porosity is
24  used, contacts 72 and 74 and feed-through 76 can be formed by
25  a single printing operation with conductive ink on one side
26  of the TYVEX sheet. Due to the porosity of the TYVEX, the ink
27  will penetrate to the other side of the TYVEX and form both
28  contacts and feed-through in one operation.
29      For probe 62 in the embodiment of Fig. 3A, substrate 68
30  is replaced by a relatively rigid PC board which includes
31  conducting wires to attach each of electrical contacts 72 to
32  one of the pins of connector 51 (Fig. 3A) and the rest of the
33  connecting structure of Fig. 5A may be omitted. It should be
34  noted that the choice of using the structure of Figs. 3A or
35  3B (i.e., probes 62 or 62') is an economic one depending on
36  the cost of manufacture of the probes. While probe 62 is
37  structurally simpler, the disposable portion of probe 62' is
38  believed to be less expensive to manufacture in large
39  quantities. Since it is envisioned that the probes will be

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1 used in large quantities and will preferably not be reused,
2 one or th other may be preferable.
3     The other side of the probe is also protected by a cover
4 plate 88 (Figs. 5A and 5B) which is attached using any bio-
5 compatible adhesive to the outer edges of dividers 66 (Fig.
6 5A) and/or to the hydrogel, which is preferably moderately
7 tacky. In one preferred embodiment of the invention, the
8 inner surface of the cover plate 88 is provided with an
9 electrically conductive layer so that the impedance of each
10 sensing element from the outer surface of the hydrogel (or
11 conductive gel) to contact 82, can be measured using an
12 external source. In addition, if a known impedance is
13 connected between the conductive layer and a reference point
14 or a source of voltage, the sensing elements can be tested in
15 a measurement mode similar to that in which they will finally
16 be used.
17     Alternatively, a film RC circuit or circuits may be
18 printed on the inner surface of plate 88 to simulate an
19 actual impedance imaging situation. Alternatively, plate 88
20 may be provided with contacts at each sensing location, and
21 circuitry which may simulate a plurality of actual impedance
22 imaging situations. Such circuitry may include external or
23 integral logic such as programmable logic arrays and may be
24 configurable using an external computer interface. The
25 simulation may provide a distinct RC circuit for each sensing
26 element or may provide a sequence of different circuits to
27 each sensing element to simulate the actual range of
28 measurements to be performed using the probe.
29     Fig. 5B shows a preferred embodiment of cover sheet 88
30 (indicated on the drawing as 88') and its mode of attachment
31 to both the multi-element sensor and the PC board. In this
32 embodiment a multi-element probe 62" is optionally further
33 attached to PC board 80 by an adhesive frame 210 which may be
34 conductive or non-conductive, and which assists in preventing
35 entry of water or gel under sensor 62". Sensor 62" is
36 preferably further aligned to PC board 80 by one or more
37 holes 222 with one or more pins 204, which are permanently
38 attached to PC board 80 or to a surface adjacent to PC board
39 80. While pin 204 is shown as being round, using rectangular,

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1 triangular, hexagonal pyramidical or other shapes provides
2 additional alignment of the sensor. In general th upper
3 portion of the pin should be curved for improved electrical
4 contact as described below.

5 The upp r exposed surface of pin 204 is conductive,
6 preferably curved and is preferably connected to a signal
7 reference source by a conductor 202 in PC board 80. Cover
8 sheet 88' is made of a single integral sheet of easily
9 deformable polyethylene, Mylar or other suitable plastic.
10 Cover sheet 88' is preferably removably attached to the upper
11 side of multi-element probe 62" by a continuous frame of
12 adhesive 225, which need not be conductive, but which seals
13 around a lip where cover 88' contacts probe 62" to protect
14 the quality and sterility of array 230 and to maintain the
15 moisture content of any medium filling wells 70. Cover 88'
16 is coated on the side facing probe 62" with a conductive
17 layer 231, such as any of the various metallic coatings, for
18 example, aluminum or the thin film coating described above.

19 Cover 88' is preferably formed after conductive coating,
20 by embossing, vacuforming or other means, to have depressions
21 233 in the cover located over corresponding wells 70. The
22 depressions are approximately centered on the center of the
23 wells and held a small distance "δ1" above the surface of
24 the hydrogel or gel, by means of relatively high sidewalls
25 226 which are formed at the same time as depressions 233.
26 Furthermore, the surface of cover 88' preferably has a
27 concave shape to match the rounded conductive contact surface
28 of pin 204, from which it is held at a distance "δ2".
29 Distances δ1 and δ2 are selected to minimize unintended
30 physical contact between the conductive inner surface of the
31 cover, the contacts in the wells and pin 204, for example,
32 during storage and handling prior to use, which might cause
33 corrosion over time due to electrochemical processes.

34 Distances δ1 and δ2 are also preferably selected so that
35 application of a nominal force (preferably about one
36 kilogram) against a flat outer surface 232 of cover 88', such
37 as by a weighted flat plate, will establish contact between
38 the inner coating 231 and the upper surface of pin 204 and
39 with the sensing elements or the gel in the wells.

1  By establishing this contact, the conductive inner
2  surface 231 is connected, on the on  hand to signals source
3  contact 202 and with each sensing element. If the coating is
4  conductor, the sensing elements are all excited by the
5  signal on lin  202; if it is a thin film circuit, th  contact
6  is via the thin film circuit. In either event, if line 202 is
7  excited by a signal, the signal will be transmitted to each
8  of the sensing elements, either directly, or via a known
9  impedance.
10  In either case, the multi-element array can be tested by
11  the system and any residual impedance noted and corrected
12  when the probe is used for imaging. If the residual impedance
13  of a given sensing element is out of a predetermined
14  specification, or is too large to be compensated for, the
15  multi-element probe will be rejected. Furthermore, the
16  computer may be so configured that imaging may only take
17  place after determination of the contact impedance of the
18  sensing elements or at least of verification that the probe
19  impedances are within a predetermined specification.
20  While pin 204 is shown as being higher than the top of
21  the wells, the pin may be at the same height as the wells, or
22  even below the wells with the cover being shaped to provide a
23  suitable distance "62" as described above.
24  In an alternative embodiment of the invention, the
25  contact surface corresponding to pin 204 is printed on  or
26  attached to the surface holding the sensing elements, with
27  contact to the PC board being via a through contact in
28  substrate 68, as for the sensing elements.
29  In yet another embodiment of the invention, the
30  conductive contact surface associated with pin 204 is on the
31  surface holding the sensing elements adjacent to pin 204. Pin
32  204 supports this surface and contacts the contact surface
33  via one, or preferably a plurality of through contacts. Pin
34  204 is designed to match the contour of the contact surface
35  and preferably, by such matching, to provide additional
36  alignment of the probe on the PC board.
37  To avoid drying out of the Gel or other potential
38  hazards of limited shelf life, the quality of any of the
39  aforementioned versions of the disposable electrode arrays

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1 can be assured by incorporating an identification code,
2 preferably including manufacturer and serial number
3 information and dat of manufacture. In a preferred
4 embodiment, the information is coded in a bar code printed on
5 each disposable probe, which is packaged together with at
6 least one other such probe (typically 5-50 probes) in the
7 same packet, which also has the same bar code. A bar code
8 reader, interfaced with the system computer, reads the
9 manufacturing information on the packet and each probe,
10 checking for date and compliance and permitting recording
11 only for a number of patients equal to the number of probes
12 in the packet.

13 In a preferred embodiment of the invention a bar code
14 may be placed on the individual disposable electrode arrays
15 which can be read by a bar code reader installed in or under
16 the PC board, for example near reference numeral 83 of Fig.
17 5B.

18 While the invention has been described in conjunction
19 with the preferred embodiment thereof, namely a generally
20 flat, somewhat flexible structure, suitable for general use
21 and for breast screening, other shapes, such as concave
22 structures (e.g., brassiere cups) or the like may be
23 preferable, and in general the shape and configuration of the
24 detectors will depend on the actual area of the body to be
25 measured. For example cylindrical arrays can be useful in
26 certain situations, for example in intra-rectal examinations
27 of the prostate or colon or inside vessels. In this context,
28 a probe according to the invention is also useful for
29 measurements inside the body, for example gynecological
30 measurements or measurements in the mouth, where the probe is
31 inserted into a body cavity and contacts the lining of the
32 cavity, and probes having shapes which correspond either
33 flexibly or rigidly to the surface being measured can be
34 used. For example, a multi-element probe in accordance with
35 the invention may be incorporated into or attached to a
36 laparoscopic or endoscopic probe.

37 Furthermore, sterilized probes can be used in invasive
38 procedures in which the probe is placed against tissue
39 exposed by incision. In this context, the term "skin" or

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1  "tissue surfac" as used herein includes such cavity lining
2  or exposed tissu surfac.
3       In a preferred embodiment of the invention, PC board 80
4  and as many elements as possible of probe 62' (or the board
5  of probe 62) are made of transparent or translucent material,
6  so as to provide at least some visibility of the underlying
7  tissue during placement of probe 62. Those elements of the
8  probe and conductors in the PC board, to the extent that they
9  are opaque should be made as small as practical to provide
10 the largest possible view to a technician or clinician to aid
11 in placement of the probe. Furthermore, probe 62 is slidably
12 displaceable when used with the above-mentioned conductive
13 gel to permit moderate lateral adjustment of the probe
14 position, to aid in placement, to ensure good contact between
15 each element and the tissue surface to be measured, and to
16 enable the user to rapidly verify whether detected
17 abnormalities are artifacts due to poor contact or are
18 genuine objects, since artifacts remain stationary or
19 disappear entirely when the probe is moved while genuine
20 objects just move in a direction opposite to the direction of
21 movement of the probe.
22      The general shape and size of the multi-element probe
23 and the size of the conductive sensing elements will depend
24 on the size of the area to be measured and on the desired
25 resolution of the measurement. Probe matrix sizes of greater
26 than 64 x 64 elements are envisioned for viewing large areas
27 and probes which are as small as 2 x 8 elements can be useful
28 for measuring small areas. Element size is preferably between
29 2 mm square and 8 mm square; however, larger sizes and
30 especially smaller sizes can be useful under certain
31 circumstances. For the breast probe 62 described above, 24 x
32 32 to 32 x 40 elements appear to be preferred matrix sizes.
33      Fig. 6A shows a perspective view of a hand held probe
34 100 in accordance with a preferred embodiment of the
35 invention. Probe 100 preferably comprises two probe heads, a
36 larger head 102 and a zoom sensor head 104. A handle 106
37 connects the sensor heads, houses switching electronics and
38 provides means for holding and positioning the probes. Handle
39 106 also optionally incorporates a digital pointing device

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1  105 such as a trackball, pressure sensitive button or other
2  such joystick device. Incorporation of a pointing device on
3  the probe enabl s the operator to control the system and
4  input positional information whil keeping both hands on
5  either the probe or patient. As d scribed below, the digital
6  pointing device can be used to indicate the position on the
7  patient's body at which the image is taken.
8      Fig. 6B shows a partially expanded bottom view of probe
9  100 of Fig. 6A, in accordance with a preferred embodiment of
10 the invention. Where applicable, like parts of the probes
11 throughout this disclosure are similarly numbered. Starting
12 from the bottom of Fig. 6B, the top half of a housing 108A
13 has a well 110 formed therein. A clear plastic window 112 is
14 attached to the edge of well 110, and a printed circuit on a
15 relatively transparent substrate, such as Kapton, designated
16 by reference 80' (to show its similarity to the corresponding
17 unprimed element of Fig. 5) is placed on window 112. A
18 flexible print cable 114 connects the contacts on printed
19 circuit 62' to acquisition electronics 116. A cable 118
20 connects the acquisition electronics to the computer. A
21 second similarly constructed, but much smaller zoom sensor
22 probe head is attached to the other end of probe 100. Either
23 of the larger or smaller heads may be used for imaging.
24     A lower half of housing 108B, encloses electronics 116
25 and print 80', whose face containing a series of contacts
26 82', is available through an opening 120 formed in the lower
27 housing half 108B. A mounting frame 122 having two alignment
28 pins 124 holds print 80' in place. Mounting and connecting
29 screws or other means have been omitted for simplification.
30     A disposable multi-element probe 62', similar to that of
31 Fig. 5 is preferably mounted on the mounting frame to
32 complete the probe.
33     Fig. 7A is a perspective view of a fingertip probe 130
34 in accordance with a preferred embodiment of the invention as
35 mounted on the finger 132 of a user. Probe 130 may be
36 separate from or an integral part of a disposable glove, such
37 as those normally used for internal examinations or external
38 palpation. The fingertip probe is especially useful for
39 localizing malignant tumors or investigating palpable masses

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1 during surgery or during internal examinations. For example,
2 during removal of a tumor, it is sometimes difficult to
3 determine th exact location or extent of a tumor. With the
4 local impedance map provided by the fing rtip probe 130 and
5 the simultaneous tactile information about the issue
6 contacted by the probe, the tumor can be located and its
7 extent determined during surgery. In a like fashion, palpable
8 lumps detected during physical breast (or other) examination
9 can be routinely checked for impedance abnormality.
10 Fig. 7B shows a flexible probe array 140 which is shown
11 as conforming to a breast being imaged. Probe array 140
12 comprises a plurality of sensing elements 141 which contact
13 the tissue surface which are formed on a flexible substrate.
14 Also formed on the flexible substrate are a plurality of
15 printed conductors 142 which electrically connect the
16 individual sensing elements 141 to conductive pads on the
17 edge of the substrate. A cable connector 144 and cable 145
18 provide the final connection link from the sensing elements
19 to a measurement apparatus. Alternatively, the flexible array
20 may take a concave or convex shape such as a cup (similar in
21 shape to a bra cup) which fits over and contacts the breast.
22 The flexible substrate is made of any thin inert
23 flexible plastic or rubber, such as those mentioned above
24 with respect to Fig. 5A. Array 140 is sufficiently pliant
25 that, with the assistance of viscous gel or conductive
26 adhesive, the sensor pads are held in intimate contact with
27 the skin or other surface, conforming to its shape.
28 Fig. 8 shows an intra-operative paddle type probe 140
29 used, in a similar manner as probe 130, for determining the
30 position of an abnormality in accordance with a preferred
31 embodiment of the invention. This probe generally includes an
32 integral sensing array 143 on one side of the paddle.
33 Preferably, the paddle is made of substantially transparent
34 material so that the physical position of the array may be
35 determined and compared with the impedance map.
36 Fig. 9 shows a laparoscopic probe 150 in accordance with
37 a preferred embodiment of the invention. Probe 150 may have a
38 disposable sensing array 152 mounted on its side or the
39 sensing array may be integral with probe 150, which is

1 disposable or sterilizable.

2 Multi-element probes, such as those shown in Figs. 7, 8
3 and 9, are pref rably disposable or sterilizable as they are
4 generally are used inside the patients body in the presence
5 of body fluids. In such situations, there is generally no
6 need or desire for a conductive gel in addition to the probes
7 themselves. Generally, printed sensing elements, such as
8 those printed with silver-silver chloride ink, or sensing
9 elements formed of conductive silicone, hydrogel or of a
10 conductive sponge may be used. While in general it is
11 desirable that the sensing elements on these multi-element
12 probes be separated by physical separators 66 (as shown in
13 Fig. 5), under some circumstances the physical distance
14 between the elements is sufficient and the separators may be
15 omitted.

16 When performing a needle biopsy, a physician generally
17 relies on a number of indicators to guide the needle to the
18 suspect region of the body. These may include tactile feel,
19 X-Ray or ultrasound studies or other external indicators.
20 While such indicators generally give a reasonable probability
21 that the needle will, in fact take a sample from the correct
22 place in the body, many clinicians do not rely on needle
23 biopsies because they may miss the tumor.

24 Fig. 10 shows a biopsy needle 154, in accordance with a
25 preferred embodiment of the invention, which is used to
26 improve the accuracy of placement of the needle. Biopsy
27 needle 154 includes a series of sensing elements 156 spaced
28 along the length of the probe. Leads (not shown) from each of
29 these elements bring signals from the elements to a detection
30 and computing system such as that described below. Elements
31 156 may be continuous around the circumference, in which case
32 they indicate which portion of the needle is within the tumor
33 to be biopsied. Alternatively, the electrodes may be
34 circumferentially segmented (a lead being provided for each
35 segment) so that information as to the direction of the tumor
36 from the needle may be derived when the needle is not within
37 the tumor. Such an impedance sensing biopsy needle can be
38 used, under guidance by palpation, ultrasound, x-ray
39 mammography or other image from other image modalities

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1  (preferably including impedance imaging as described herein),
2  taken during the biopsy or prior to the biopsy to improve the
3  accuracy of placement of the needle. In particular, the
4  impedanc imag from the needle may be combined with the
5  other imag s in a display. While this asp ct of the inv ntion
6  has been described using a biopsy needl , this aspect of the
7  invention is also applicable to positioning of any elongate
8  object such as an other needle (such as a localizing needle),
9  an endoscopic probe or a catheter.
10      Returning now to Figs. 1-3 and referring additionally to
11  Figs. 11-14, a number of applications of multi-element probes
12  are shown. It should be understood that, while some of these
13  applications may require probes in accordance with the
14  invention, others of the applications may also be performed
15  using other types of impedance probes.
16      Fig. 11A shows the use of the biopsy needle in Fig. 10
17  together with an optional ultrasound imaging head in
18  performing a biopsy. A breast 160 having a suspected cyst or
19  tumor 162 is to be biopsied by needle 154. An ultrasound head
20  164 images the breast and the ultrasound image, after
21  processing by an ultrasound processor 166 of standard design
22  is shown on a video display 168. Of course, the ultrasound
23  image will show the biopsy needle. The impedance readings
24  from probe 154 are processed by an impedance processor 170
25  and are overlaid on the ultrasound image of the biopsy needle
26  in the display by a video display processor 172.
27      In one display mode, the portions, as shown in Fig. 11B
28  of the needle which are within the tumor or cyst and which
29  measure a different impedance from those outside the tumor,
30  will be shown in a distinctive color to indicate the portion
31  of the needle within the tumor or cyst. In a second display
32  mode, the impedance measured will be indicated by a range of
33  colors. In yet a third embodiment of the invention, in which
34  circumferentially segmented sensing elements are employed,
35  the impedance processor will calculate radial direction of
36  the tumor from the needle and will display this information,
37  for example, in the form of an arrow on the display.
38      The image sensing biopsy needle can also be used with
39  one or more imaging arrays (28, 30) such as those shown in

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1  Fig. 6 or Fig. 3B to impedance image the region to be
2  biopsied during the biopsy procedure. Alternatively, at least
3  one of th  arrays can be an imaging array of the non-
4  imp dance type. In one pref rred embodiment, shown in Fig.
5  11C, the needle is inserted through an aperture (or one of a
6  plurality of apertures) 174 in a multi-element probe which is
7  imaging the region. The region may, optionally, be
8  simultaneously viewed from a different angle (for example at
9  90° from the probe with the aperture) with an other impedance
10  imaging probe. In the case that both arrays 28 and 30 are
11  impedance imaging arrays, the biopsy needle or other elongate
12  object can either have impedance sensing or not, and the two
13  images help direct it to the region. The probe with one or
14  more apertures is sterile and preferably disposable. This
15  biopsy method is shown, very schematically, in Fig. 11C.
16      In an alternative preferred embodiment of the invention,
17  only the perforated plate through which the needle or
18  elongate object is passed is an imaging array. In this case
19  the array through which the needle passes give a two
20  dimensional placement of the impedance abnormality while an
21  imaging or non-imaging impedance sensor on the needle gives
22  an indication of when the needle has reached the region of
23  impedance abnormality, as described above.
24      Alternative guiding systems for frontal and lateral
25  breast biopsy or for guiding an elongate element to a desired
26  impedance region of the body are shown in Figs. 11D and 11E,
27  respectively.
28      Fig. 11D shows a system for in which two relatively
29  large plate multi-element probes 28, 30 are placed on
30  opposite sides of the desired tissue, shown as a breast 160
31  of a prone patient 161. Sensor array probes 28 and 30 are
32  held in position by positional controller 181 via rotatable
33  mounts 191. A mount 198 positions a biopsy needle 199 within
34  the opening between probe arrays 28 and 30, and is operative
35  to adjust its height. A suspicious region 183 which is
36  located at positions 184 and 185 on arrays 28 and 30
37  respectively as described herein, which information is
38  supplied to a CPU 197, which determines the position of the
39  suspicious region for controller 181. The controller then

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1  inserts the needle into the suspicious region, for example,
2  to take the biopsy. Biopsy needle 199 is preferably of the
3  type shown in Fig. 10 to furth r aid in positioning of the
4  n edle. As indicated above, this is not required for some
5  embodiments of the invention.
6      Alternatively, biopsy needle 199 may be inserted through
7  holes formed between the elements of probes 28 and/or 30 as
8  described above. Furthermore, while automatic insertion of
9  the biopsy needle is shown in Fig. 11D, manual insertion and
10 guidance based on impedance images provided by the probes is
11 also feasible.
12     Fig. 11E shows a system similar to that of Fig. 11D in
13 which the imaging and biopsy needle insertion is from the
14 side of the breast, rather than from the front. Operation of
15 the method is identical to that of Fig. 11D, except that an
16 additional probe 29 may be provided for further localization
17 of suspicious region 183. Alternatively, one or two of the
18 probes may be substituted by plates of inert material for
19 holding and positioning the breast.
20     It should be noted that while the breast has been used
21 for illustrative purposes in Figs. 11A through 11E, the
22 method described is applicable to other areas of the body,
23 with necessary changes due to the particular physiology being
24 imaged.
25     It should be understood that one or more of the elements
26 on the needle may themselves be electrified to cause them to
27 "light-up" on the image. This electrification may be AC or DC
28 may be the same or different from the primary image stimulus,
29 may have a single frequency or a complex form and may be
30 applied in a continuous or pulsed mode. If one or more of the
31 sensing elements is used in this manner, said elements are
32 preferably alternatively used to apply an electrification
33 signal and to function as sensors, i.e., to sense signals
34 from the primary stimulus.
35     Fig. 12 shows, very schematically, the intra-operative
36 probe of Fig. 8 combined with a video camera 256 to more
37 effectively correlate the impedance measurement with the
38 placement of the probe on the body. An intra-operative probe
39 140 preferably having a number of optically visible fiduciary

1  marks 146 is placed on the suspect lesion or tissue. A video
2  camera 256 sequentially views the area without the probe and
3  th  same ar a with the probe in place and displays a
4  composit image on a video display 258 after processing by a
5  processor 260. Processor 260 receives the impedanc data from
6  probe 140, determines the positions of the fiduciary marks
7  from the video image and superimposes the impedance image on
8  the video image, with or without the probe, which is
9  displayed on display 258.
10      Fig. 13 shows a laparoscopic or endoscopic probe 250
11 used in conjunction with a fiber-optic illuminator/imager
12 252. In this embodiment, the laparoscopic impedance probe,
13 which is formed on a flexible, preferably extendible paddle,
14 is viewed by the illuminator/imager which is preferably a
15 video imager, which is well known in the art. Probe 250 can
16 be either round or flat, depending on the region to be
17 imaged. When the imager views a suspicious lesion or tissue,
18 probe 250 is extended to determine the impedance properties
19 of the lesion. The combination of probe 250 and imager 252
20 may be incorporated in a catheter 254 or other invasive
21 element appropriate to the region of the body being
22 investigated.
23      Optically visible fiduciary marks 253 on probe 250 are
24 preferably used to determine the position of probe 250 within
25 the video image of the tissue seen by fiber-optic
26 illuminator/imager 252, in a manner similar to that discussed
27 above with respect to Fig. 12.
28      In a preferred embodiment of a system using any of the
29 biopsy needle, intra-operative probe, finger tip probe or
30 other embodiments described above, an audible sound
31 proportional to an impedance parameter measured by the needle
32 or other sensor in or on the body is generated by the system
33 computer. This feature may be useful in situations where the
34 probe is placed in locations which are difficult to access
35 visually, such as suspected lesions during surgery. Such an
36 audible sound could include any kind of sound, such as a tone
37 whose frequency is proportional to the measured parameter or
38 similar use of beeps, clicks, musical notes, simulated voice
39 or the like. This feature can also be used for non-surgical

1  procedures such as rectal, vaginal or oral examinations, or
2  other examinations.
3      Fig. 16 shows methods useful for estimating the depth
4  of a lesion and also for determining if a image contains a
5  true lesion or an artifact.
6      A breast or other region 160 is imaged by a probe 270,
7  for example, the probe of Figs. 1-3 or Figs. 6A and 6B. The
8  depth of a local impedance deviation can be estimated by
9  palpating the breast or other region by a finger 272 or a
10 plunger 274. The displacement of the local deviation on the
11 image will be maximized when the palpation is at the same
12 level as the lesion. It should also be understood that, where
13 palpation causes movement of the local deviation on the
14 impedance image, this is an indication that the deviation is
15 "real" and not an artifact.
16     In a similar manner, application of variable compression
17 to the imaging probe will result in a variation of the
18 distance from the probe to deviation under the probe. This
19 distance variation will cause a corresponding variation in
20 the size and intensity of the deviation, thus helping to
21 verify that the deviation is not artifactal.
22     Alternatively or additionally, the probe can be moved
23 along the surface of the tissue without moving the tissue. In
24 this case, surface effects will have a tendency to either
25 disappear or to move with the probe (remain stationary in the
26 image) while real anomalies will move, on the image, in the
27 opposite direction from the movement of the probe.
28     Alternatively or additionally, the probe and the tissue
29 can be moved together without moving the underlying structure
30 (such as the bones). Tissue lesions will remain relatively
31 stationary in the image while bone artifacts will move in the
32 opposite direction.
33     In operation, a system according to the present
34 invention measures impedance between the individual sensing
35 elements and some reference point (typically the signal
36 source point) at some other place on the body. Generally, in
37 order to produce an interpretable impedance image, the
38 sensing elements in the multi-element probe should detect
39 distortions in the electric field lines due solely to the

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1 presence of a local impedance difference between embedded
2 tissue of on   type (for exampl , a tumor) and surrounding
3 tissue of anoth r type (for example, normal adipose tissue).
4     To avoid distortion in the field lines, the reference
5 point is typically placed far from the sensor array, all
6 sensing elements are all at ground or virtual ground, and the
7 current drawn by the elements is measured. Since the probe is
8 at ground (an equipotential) the electric field lines (and
9 the current collected by the elements) are perpendicular to
10 the surface of the multi-element probe. In principle, if
11 there are no variations of impedance below the probe, each
12 element measures the integrated impedance below the element.
13 This first order assumption is used in the determination of
14 the position and/or severity of a tumor, cyst or lesion. It
15 is clear, however, that the multi-element probe covers only a
16 portion of even the organ which is being imaged. The area
17 outside the area of the probe is not at ground potential,
18 causing the field lines to bend out at the periphery of the
19 probe, biasing the edge of the impedance image.
20     To reduce this effect, a conductive "guard ring" is
21 provided around the edge of the imaged area to draw in and
22 straighten the field lines at the edge of the imaged area.
23 This guard ring, if one is desired, can consist of merely
24 ignoring the, presumably distorted, currents drawn by the
25 elements at (or near) the edge of the probe and ignoring the
26 measurements made by these elements. In general, while the
27 use of a guard ring reduces the edge effect at the edge of
28 the field, it is still generally necessary to determine
29 values for comparison or determination of polychromic values
30 near the ring based only on pixels near the ring and not on
31 the image as a whole.
32     Furthermore, to possibly reduce the baseline impedance
33 contributed to the local impedance image by tissue between
34 the remote signal source and the region near the probe, an
35 additional reference electrode may be placed on the patient's
36 body relatively near the multi-element probe. For example, if
37 the source is placed at the arm of the patient and the breast
38 is imaged from the front, a reference electrode for sensing a
39 reference voltage can be placed at the front of the shoulder

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1  of the patient. The measured impedances ar  then reduced by
2  the  impedance  value  of  the  refer nce  electrode.
3  Alternatively, the impedance values of the elements of the
4  multi-element probe are averaged to form a reference
5  impedance, and the display of th  impedance map is corrected
6  for this reference impedance.
7      One way to substantially avoid at least some of the
8  above- mentioned problems is to use the apparatus shown in
9  Figs. 1-3. As indicated above, the apparatus incorporates two
10  probe heads 28 and 30. The breast to be imaged is placed
11  between the probe heads and the breast is compressed by the
12  heads (although generally to a lesser degree than in X-Ray
13  mammography) so that the breast forms a relatively flat
14  volume and fills the region between the probes. It should be
15  noted that, if the current is measured at each of the sensing
16  elements in both probes, then two somewhat different images
17  of the same region are generated. Avoidance of the problems
18  also results when the two multi-element probes are not
19  parallel as described above.
20      It should be noted that when used on breasts, the images
21  produced by the pair of large, flat probes of Fig. 3 have the
22  same  geometric  configuration  as  standard  mammograms.
23  Furthermore if used in the same compression orientations, the
24  impedance  images  can  be  directly  compared  to  the
25  corresponding mammograms. In one preferred embodiment of the
26  invention, mammograms corresponding to the impedance images
27  to be taken are digitized, using film scanning or other
28  digitization means known in the art, and entered into the
29  system computer. If the mammogram is already digital, such as
30  may be provided by a digital mammogram, the image file can be
31  transferred from the mammogram.
32      The mammograms and impedance images can be overlaid or
33  otherwise combined to form a single image. Such an image
34  could highlight those areas of the mammogram in which the
35  impedance is particularly low or high. Such a combined image
36  thus presents two independent readouts (impedance and
37  radiographic density) of the same well defined anatomical
38  region in a known geometric orientation, to facilitate
39  interpretation, correlation with anatomy and localization.

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1 It is well known that the resolution of objects in an
2 impedance image is reduced with distance of the object from
3 the probe. Thus, it is possible to estimate the distance of
4 the object from th two probes based on the relative size of
5 the same object on th two different probes. As indicated
6 above, two opposing views of the breast may be taken. This
7 would provide further localization of the object.
8 In one mode, the sensing elements of one probe are all
9 electronically floating while the elements of the other probe
10 are at a virtual ground (inputs to sensing electronics), and
11 a remote signal source is used, as previously described.
12 After an image is obtained from the one probe, the roles of
13 the two probes are reversed to obtain an image from the other
14 probe.
15 Alternatively, if all of the elements of one of the flat
16 probes are electrified to the same voltage and the measuring
17 probe is kept at virtual ground, the currents drawn from and
18 received by the elements of both probes form a two
19 dimensional admittance image of the region between the
20 probes.
21 In a further preferred embodiment of the invention, one
22 or a few closely spaced sensing elements on one of the probes
23 is electrified, and the others are left floating. This would
24 cause a beam-like flow of current from the electrified
25 elements to the other sensing elements on the other probe.
26 The object would disturb this flow causing impedance
27 variations which are strongest for those elements which are
28 in the path of the current disturbed by the object. If a
29 number of such measurements are made with, each with a
30 different group of electrodes being electrified, then good
31 information regarding the position of the object can be
32 obtained.
33 In practice, as indicated above, orthogonal views of the
34 breast are taken giving additional position information.
35 In preferred embodiments of the invention the breast is
36 imaged at a plurality of frequencies and both the real and
37 imaginary parts of the impedance are calculated. The
38 sensitivity of the detection of malignant tissue is a
39 function of frequency, and, for a particular frequency, is a

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1  function of th impedance measure or characteristic used for
2  imaging, for example, real part of th impedance (or
3  admittance), imaginary part of the imp dance (or admittance),
4  absolut value of the impedance (or admittance), phase of the
5  impedance (or admittance), the capacitance or some function
6  of the impedance or of admittance compon nts.
7      In a practical situation, an impedance measure should
8  give the maximum contrast between a malignancy and non-
9  malignant tissue. It is therefore desirable to determine the
10 frequency or combination of frequencies which give maximum
11 detectability and to determine it quickly. One method of
12 determining the frequency is to perform swept frequency
13 measurements and to use the frequency or combination of
14 frequencies which results in the best contrast.
15 Alternatively, a number of images taken at relatively close
16 frequencies can be used. It is believed that for many
17 purposes, at least four samples should be taken in the range
18 between and including 100 and 400 Hz and, preferably, at
19 least one or two additional images are taken at frequencies
20 up to 1000 Hz.
21      A second method is to use a pulsed excitation and
22 Fourier analysis to determine impedance over a range of
23 frequencies. The optimum frequency or frequencies determined
24 from the swept or pulsed measurement are then used in a
25 single or multiple frequency measurement. A pulse shape which
26 has been found useful in this regard is a bi-polar square
27 pulse having equal positive and negative going pulses of 5-10
28 millisecond duration and fast rise and fall times.
29      A number of measures of the impedance, as described
30 below, have been found useful for comparing different areas
31 of the image. Generally, it is useful to display a gray scale
32 or pseudo-color representation of the values of the impedance
33 measure, either on a linear scale or where the square of the
34 impedance measure is displayed. Also useful is an "absorption
35 scale" where the value of an impedance measure, v, is
36 displayed as:
37      $$d(v)=(max-1)*(exp(v*(max-1)-1))/(e-1),$$
38 where max is the maximum normalized value of v. Generally,
39 the display is most useful when the measure is normalized,

1 either by division or subtraction of the minimum or average
2 value of the measure in the display or the estimated standard
3 deviation or other measure of variance for the image.
4     Furthermore, the display may be automatically windowed
5 to include only those values of the impedance measure
6 actually in the image, or to include a relative window of
7 selectable size about the average value of the impedance
8 measure. The range of values to be displayed may also be
9 determined using a baseline average value measured at a
10 region remote from irregularities, i.e., remote from the
11 nipple of the breast. Alternatively, the baseline average may
12 be a predetermined average value as measured for a large
13 group of patients. Alternatively, a reference region on the
14 image may be chosen by the user to determine the baseline
15 average to be used for windowing.
16     While the display may show the exact measure for each
17 pixel as is conventional, for example, in displays of nuclear
18 medicine images, in a preferred embodiment of the invention
19 the display is an interpolated image formed by quadratic or
20 cubic spline interpolation of the impedance measure values.
21 This type of display removes the annoying checkerboard effect
22 of the relatively low resolution impedance image without any
23 substantial loss of spatial or contrast detail.
24     The measures of impedance which have been found useful
25 for comparing different areas of the image may be grouped as
26 single frequency measures and polychromic measures.
27     Single frequency measures include the admittance,
28 capacitance, conductance and phase of the admittance and its
29 tangent. These measures may be measured at some predetermined
30 frequency, at which the sensitivity is generally high, or at
31 a frequency of high sensitivity determined by a preliminary
32 swept or pulsed measurement. Cancer typically has
33 significantly higher phase than the average surrounding
34 tissue, with greatest difference at low frequencies such as
35 100 Hz, but often significant up to 5 KHz.
36     Polychromic impedance measures are based on measurements
37 at more than one frequency, such as on a spectral curve based
38 on fitting a set of capacitance (C) and conductance (G)
39 values determined at a plurality of frequencies using linear

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1  interpolation, quadratic interpolation, cubic spline, band
2  limited Fourier coefficients, or other methods known in the
3  art.
4       One polychromic measure is a spectral width measure. For
5  a given pixel or region of interest the value of C parameter
6  falls (and the G parameter rises) with frequency. The
7  spectral width of the spectrum is the width to a given
8  percentage fall in the C value as compared to the value at
9  some low frequency, for example 100 Hz. If the parameter does
10 not fall by the given percentage in the measured range it is
11 assigned an impedance measure equal to the full measured
12 bandwidth. Similarly, the spectral width of the G-spectrum is
13 the width to a given rise in the G-Parameter compared to the
14 value at some low frequency, for example 100 Hz, or
15 alternatively, the fall in G with decreasing frequency
16 compared to the value at some high frequency, for example
17 3000 Hz.
18      A second polychromic measure is a spectral quotient in
19 which the impedance measure is the ratio of the measured
20 value of G or C parameters at two preset frequencies, which
21 may be user selected, or which may be selected based on the
22 swept or pulsed measurements described above. This measure,
23 as all of the others may be displayed on a per-pixel basis or
24 on the basis of a region of interest of pixels, chosen by the
25 user.
26      A third type of polychromic measure is based on a
27 Relative Difference Spectrum determination. In this measure,
28 the capacitance or conductance for a given region of interest
29 (or single pixel) is compared to that of a reference region
30 over the spectrum to determine a numerical difference between
31 the two as a function of frequency. The thus derived Relative
32 Difference Spectrum is then analyzed. For example, a spectral
33 width measure as described above has been found to be a
34 useful measure of abnormalities. Normally the width is
35 measured where the relative difference spectrum passes from
36 positive to negative, i.e., where the C or G is equal to that
37 of the reference region. For capacitance, this spectrum width
38 is designated herein as the Frequency of Capacitance
39 Crossover (FCX). This measure has been found to be especially

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1  useful in classification of tissue types as described below.

2  A fourth type of polychromic measure is based on a
3  Relative Ratio Spectrum determination. This is similar to the
4  Relative Difference Spectrum, except that the ratio of the
5  values between the referenc  area and the region of interest
6  is used. A spectral width measure can be determined for this
7  spectrum in the same manner as for the Relative difference
8  Spectrum. Normally, the width is measured where the ratio is
9  1. This width is the same as the width of Relative Difference
10  Spectrum at the zero (cross-over) point.

11  A fifth type of polychromic measures are the Positive
12  and Negative Integrated Relative Difference for Capacitance
13  and/or Conductance abbreviated C (for capacitance) or G (for
14  conductance) NIRD or PIRD. These values are calculated by
15  adding up the negative (or positive) deviations of the
16  capacitance (or conductance) values in the area of
17  abnormality from those of a representative value (or range of
18  values) of the capacitance (or conductance) at the various
19  measured frequencies. This representative value or range is
20  determined from pixel values in the image selected to exclude
21  exceptionally high or low capacitance (or conductance)
22  values. The same pixel may have both a C-NIRD and a C-PIRD if
23  its capacitance deviates positively from the representative
24  value for some subset of the frequencies and negatively from
25  the representative value for a different subset of the
26  frequencies. The C-NIRD, C-PIRD and G-NIRD measures have been
27  found to be especially useful for characterizing tissue type
28  as described below.

29  A sixth polychromic measure is the integrated phase. For
30  a given pixel in the image, the phase is measured at a
31  plurality of frequencies in a desired frequency range,
32  typically 100 to 5000 Hz. The integrated phase is the sum of
33  the phase over a number of frequencies, typically about 13
34  frequencies between 100 and 3200 Hz. Alternatively,
35  integration may be performed using the trapezoidal rule or by
36  integrating another functional fit to the sampled values in
37  the desired frequency range. Cancer typically has
38  significantly higher integrated phase. The integrated tangent
39  of the phase is an alternative measure of this measure.

A seventh polychromic measur is the integrated phase difference. In a given image, the phase of each pixel is measured at each of a plurality of frequencies in a desired frequency range, typically 100 to 5,000 Hz and th median or average phase determined for the image at each frequency. In calculating the median or the average, the highest and lowest values are preferably excluded by using such methods as (1) including only pixels whose values lie within a specified range of the pixel histogram, such as only those between the 25 and 75 percentile phase values for the image. For each frequency, the median or average for the image is subtracted from the phase value for each pixel. This results in a phase difference spectrum which is positive for frequencies where the pixel value is higher than average and negative where it is lower. The sum of the phase differences is the integrated phase difference (IPD), and the sum of all the positive phase differences is the integrated positive phase difference. Both these measures are significantly higher for cancer than for normal surrounding tissues.

An eighth polychromic measure is the specific frequency. The phase of each pixel is measured at each of a plurality of frequencies in a desired frequency range, typically 100 to 5000 Hz. The resultant spectrum is fitted to a piecewise linear function, a spline function or a functional fit as known in the art. The lowest frequency at which the phase reaches 45 degrees is defined as the Specific Frequency. Specific Frequency is typically lower for cancer (range of 100 to 800 Hz) than for normal surrounding tissue (range of 1200 Hz to several kilohertz. The RC time constant evaluated at the specific frequency is also a useful related polychromic measure, being lower for cancer.

A ninth polychromic measure is the capacitance spectral slope, i.e., the derivative of the capacitance curve (or of the log capacitance curve). as a function of frequency, evaluated at a given frequency. This is considered to be a polychromic measure, since its determination requires the measurement of the capacitance at more than one point. Capacitance Spectral slope in the range 100 to 5000 Hz is typically negative and typically has a higher absolute value

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1 in cancer vs. normal pixels, particularly at low frequencies

2 such as 100 to 500 Hz.

3 A tenth polychromic measure is the conductance spectral

4 slope, the d rivative of the conductance (or of the log

5 conductance) evaluated at a given frequency. Conductanc

6 Spectral slope in the range 100 to 5000 Hz is typically

7 positive and typically has a lower value in cancer vs. normal

8 pixels, particularly at low frequencies such as 100 to 500

9 Hz.

10 The NIRD and PIRD measures may be defined in various

11 ways. For example, the deviations from the representative

12 value may be used in the calculation only when they exceed

13 some minimum value. The deviation may be expressed as a the

14 actual numerical deviation or more preferably as a ratio or

15 as a deviation normalized to some "standard" deviation of the

16 capacitance or conductance which is characteristic of normal

17 tissue, as defined below.

18 Preferably, the value representative of normal tissue is

19 derived by looking at pixel values representative of some

20 proportion of the total number of pixels in an image. For

21 example if a 8x8 image were used, and the anomalous portion

22 occupied less than 25% of the image, the 16 pixels having

23 each of the highest and the lowest values would not be

24 considered. The representative value would then be, for

25 example, the mean value of capacitance or conductance of the

26 remaining pixels and a standard deviation would be the range

27 of pixel values among the 32 pixels which are considered.

28 This determination is based on the practical

29 consideration that almost always at least 50% of the pixels

30 represent normal tissue. It is clear that many other measures

31 of the representative value and of the "standard" deviation

32 will be equally useful in the practice of the invention and

33 that such measures may be computed in many different ways.

34 Furthermore the range of pixels which are considered "normal"

35 may be adjusted depending on the type of tissue actually

36 being measured. For example, for tissue having large areas

37 with apparently high values, a range of pixel values such as,

38 for example 20%-50% (instead of the 25%-75% described above)

39 may be more useful.

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Another potentially useful polychromic parameter is the slope of the logarithm of the capacitance of a given pixel or region as a function of frequency. This curve generally has a shape which is predominantly linear. Alternativly, the ratio of the slope of the capacitance of the particular pixel to the slope of the capacitiv repres ntative value may be useful.

Furthermore, it may be useful to consider, as an additional polychromic measure, the maximum of one of the other polychromic measures, for example, the capacitance, conductance, Relative Difference Spectrum, Relative Ratio Spectrum, etc.

In general, some pixels are excluded from the characterization. These would include "No-Contact" pixels having near zero conductance and capacitance values and "Contact Artifactal Hot Spots" which are pixels, with elevated capacitance or conductance values, next to no contact pixels.

In impedance measurements of the breast in both men and women, normal breast tissue has a low capacitance and conductivity, except in the nipples, which have a higher C and G values than the surrounding tissue with the maximum obtained at the lowest frequency recorded, typically 100 Hz. The nipple capacitance and conductance remains very much higher than the surrounding tissue up to about 1400 Hz for fertile patients and up to about 2500 Hz for older patients (which is reduced to 1400 Hz for older patients by estrogen replacement therapy). These frequencies represent the normal range of spectral widths for the Relative and Difference Spectra. Tumors can be recognized by very high C and G relative ratio or relative difference values at all frequencies below 1000 Hz and moderate difference or ratio values for frequencies up to 2500 Hz or even higher.

Capacitance and conductance values are measured by comparing the amplitude and phase of the signal received by the sensing elements. Knowing both of these measures at the same points is useful to proper clinical interpretation. For example, as illustrated below in Fig. 14, a region of elevated conductivity and reduced capacitance (especially at

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1 relatively low frequencies, most preferably less than 500 Hz,
2 by generally below 2500 Hz and also below 10 kHz) is
3 associated with benign, but typically pre-cancerous atypical
4 hyperplasia while, as shown in Fig. 15, canc r typically has
5 both elevated capacitance and conductivity over, generally, a
6 wide frequency range, as compared to the surrounding tissue.
7 Proper differential diagnosis is aided by having the
8 frequency samples be close enough together so that changes in
9 the conductivity and capacitance in the low frequency range
10 can be tracked. This also requires the display of both
11 capacitance and conductance or the use of an impedance
12 measure which is based on an appropriate combination of the
13 two.
14     Methods for calculating C and G are given in the
15 abovementioned US patents 4,291,708 and 4,458,694, the
16 disclosures of which are incorporated herein by reference. A
17 preferred embodiment of the invention takes advantage of the
18 calibration capability inherent in the use of cover plates as
19 shown in Figs. 5A and 5B. It can be shown that if the
20 received waveform is sampled at a fixed spacing, $\delta$, such
21 that N samples are taken in each cycle, then the real and
22 imaginary values of the impedance can be determined as:

23

$$G = \Sigma(g_n(V_{(n+\frac{1}{2}N)} - V_n),$$
24

25 and

$$\omega C = \Sigma(c_n(V_{(n+\frac{1}{2}N)} - V_n),$$
26

27 where $g_n$ and $c_n$ are constants determined by a calibration
28 procedure and $V_n$ is the voltage measured at the nth sampling
29 point (out of N). The first sample is taken at zero phase of
30 the reference signal.
31     One relatively easy way to determine the constants is to
32 perform a series of measurements when cover plate is in
33 contact with the sensing elements as described above and a
34 known impedance is placed between the transmitter and the
35 cover plate. Since N coefficients are required for
36 determining $g_n$ and $c_n$ for each frequency, N values of
37 admittance and N measurements are required. For example, if
38 N=4 (four samples per cycle) four different measurements are
39 taken and the sampled signal values are entered into the

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1 above equations to give N quations, which are then solved
2 for the values of the coefficients. The higher the number of
3 samples, the greater the accuracy and noise immunity of the
4 syst m, however, the calibration and computation times are
5 increased.
6 Alternatively, fewer samples are taken and values for a
7 number of measurements are averaged, both in the calibration
8 and clinical measurements to reduce the effects of noise.
9 Artifactal abnormalities in the impedance image can be
10 caused by such factors as poor surface contact or
11 insufficient conductive coupling on some or all of the
12 sensing elements, the presence of air bubbles trapped between
13 probe and tissue and normal anatomical features such as bone
14 or nipple.
15 Bubbles can be recognized by their typically lower C and
16 G values compared to background, often immediately surrounded
17 by pixels with much higher C and G. Bubbles can be verified
18 and eliminated by removing the probe from the skin and
19 repositioning it, and or by applying additional conductive
20 coupling agent. Contact artifacts can be determined and
21 accounted for in real time by translating the probe and
22 viewing the image as described above. Artifacts either
23 disappear or remain fixed with respect to the pixels, while
24 real tissue features move, on the image, in a direction
25 opposite from the motion of the probe. Additionally, as
26 described above, if the tissue beneath the skin is physically
27 moved, while the probe and skeletal structure is kept fixed,
28 only real tissue features will move. If the feature remains
29 static, it is either a skin feature or bone.
30 If as described above, the probe and the tissue are
31 moved together without moving the underlying structure (such
32 as the bones). Tissue lesions and surface effects will remain
33 relatively stationary in the image while bone artifacts will
34 move in the opposite direction, thus distinguishing them from
35 other impedance deviations.
36 Fig. 14 shows one example of a display, according to a
37 preferred embodiment of the invention. In this display,
38 capacitance and conductivity images at two positions on a
39 breast are shown, together with an indication of the

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1  positions on the breast at which these images were acquired.
2      In particular, as seen in Fig. 15, the display includes
3  the capability of displaying up to five sets of capacitance
4  and conductance images in the five sets of smaller squares.
5  These images are associated with probe areas indicated as
6  numbers 1-5 on the breast image shown in the display. In
7  practice, the examiner manipulates a joystick or other
8  digital pointing device, such as device 105 shown in Fig. 6A.
9  This device is manipulated until a square is appropriately
10  placed on the breast image. The examiner then presses a
11  button which causes a pair of impedance images to be stored
12  and displayed on the screen in an appropriate square, and the
13  indicated position to be displayed on the physiological
14  (breast) drawing. The small images are numbered from left to
15  right. Preferably, the examiner can scale the physiological
16  image so that the dimensions of the breast shown and the
17  extent of the probe array are compatible. It should be
18  understood that during the placement of the probe, real time
19  images (acquired about once every 50-80 msec) of the
20  capacitance and the conductance are shown, for example in the
21  large squares to the left of the display.
22      Fig. 14, which represents an actual imaging situation
23  shows, in the leftmost of the small images, a situation in
24  which a small atypical hyperplasia which was previously
25  detected by other means. This position shows an elevated
26  conductivity and a very slightly reduced capacitance. In
27  position 2, which is also shown in the two large squares to
28  the right of the display, a previously unsuspected area
29  having a capacitance/conductance profile characteristic of
30  atypical hyperplasia is detected.
31      Fig. 15 shows a study typical of multiple suspected
32  sites of carcinoma (in positions 2 and 4). The images of
33  position 4 are shown in enlarged format at the left of the
34  image. In these sites, both the capacitance and conductance
35  are elevated with respect to their surroundings.
36      Alternatively, a composite image such as the image of
37  the sum of the capacitance and conductance images, their
38  product, their sum or their ratio can be displayed to give a
39  similar indication of the type of detected anomaly. A color

1  coded composite image can also be displayed, where, for
2  example, the median value for each image would be black and
3  wh re positive and negative values would have a particular
4  color which, when combined would result in distinctive colors
5  for suspect impedance deviations.
6      The display shown in Figs. 14 and 15 can be
7  utilized to show a plurality of images of the same region at
8  a plurality of frequencies. Alternatively or additionally,
9  the display can be utilized to show a plurality of different
10  polychromic measures of the same region. In addition, using,
11  for example, the fact, as described below with an example,
12  that a plurality of such measures can be useful in
13  identifying tissue type more accurately than can a single
14  measure, the display may include, inter alia, an image in
15  which portions of the image is identified by tissue type. For
16  such an image, for example, the color of portions of the map
17  could represent the type of tissue and the brightness the
18  certainty of the identification. The type identification and
19  certainty would depend on the probability that a particular
20  "mix" of values of the polychromic measures are associated
21  with a particular tissue type and that not all measures are
22  always within the specified range for any particular tissue
23  type. In conjunction with the display of such a map the
24  individual polychromic measures may be displayed either
25  together or in sequence to make the determination of the
26  tissue type more certain.
27      One type of display of multiple polychromic images is to
28  use a pseudo color image of two or three colors, each of
29  which represents one of the measures. When a measure for a
30  portion of the image meets the criteria for a given tissue
31  type it is displayed in its assigned color. When two or more
32  such criteria are met a different color is displayed,
33  depending on which of the criteria are met.
34      Another type of display shows the values of the measures
35  as iso-contours of varying brightness of a color assigned to
36  the measure. The conjunction of isocontour lines
37  characteristic of a given tissue type may then be recognized
38  from isocontours.
39      Alternatively or additionally, the image can be a pseudo

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1  3-D image wh rein each of the measures is delineated as a
2  wire screen of a given color. This allows for the
3  visualization of more than one measure at the same time.
4      Alternativ ly, a map of immitance, or the real or
5  imaginary part thereof is overlaid with indications, based on
6  polychromic measures of the tissue type involved, as for
7  example by color coding, by arrows with associated legends or
8  by other means to alert the operator to suspected sites of
9  tissue of specific types. Such measures may be calculated
10 automatically or in response to a query from the operator in
11 respect to an area of the image of which he is suspicious.
12     It has been found that certain immitance measures and
13 combinations of measures are characteristic of certain types
14 of normal and abnormal tissue. In one example of the method
15 four of the polychromic measures described above can be
16 utilized separately or, more particularly, in combination to
17 indicate the presence of certain normal or abnormal tissue.
18 These four measures are CFX, G-PIRD, C-PIRD and C-NIRD
19 measure. Other combinations of polychromic measures are also
20 useful in indicating tissue type.
21     It has been found that normal tissue, as expected, has
22 low or zero values of all of the measures. Nipples and the
23 infra-mammary ridge have a very high value of G-PIRD and C-
24 PIRD together with zero to low value of CFX and no G-NIRD.
25 Ribs and the costo-chondral junction have low values of C-
26 PIRD and CFX, moderate to high values of G-PIRD and low
27 values of C-NIRD. Typical benign hyperplasia has a moderate
28 to high value of C-NIRD and G-PIRD, a high value of CFX and
29 no C-PIRD, while precancerous atypical hyperplasia has values
30 in a range similar to that of typical hyperplasia for C-NIRD,
31 and G-PIRD but has a moderate value of CFX and C-PIRD. This
32 allows precancerous atypical hyperplasia to be differentiated
33 from benign hyperplasia. Furthermore, cancerous tumors appear
34 to be characterized by medium to high values of C-PIRD and
35 CFX, high values of G-PIRD and low values C-NIRD. Some
36 tumors, especially those with very high C-PIRD have no C-
37 NIRD.
38     The four measures, C-PIRD, C-NIRD, G-PIRD and CFX, form
39 a four dimensional space in which each set of measurements in

1 designated by a single point. In order to represent such a
2 space on paper two orthogonal projections of the four
3 dimensional space are required. One such s t of orthogonal
4 projections is shown in Figs. 18A and 18B. While these
5 projections fully describe all four measures, they plot the
6 measures in pairs only. Presenting the regions of the space
7 which are characterized by the various tissue types in a
8 single drawing is possible since all of the measures have
9 only positive (or zero) values. Since only positive values of
10 the measures are allowed it is possible to combine these two
11 orthogonal projections, as in Fig. 18C, into a single
12 projection in which each of the axes represents a positive
13 value of one of the measures. Fig. 18C shows the information
14 in a redundant manner (i.e., it actually shows two orthogonal
15 projections), however, it is useful since it shows all
16 combinations of the various measures on a single figure.
17 It will be noted from Figs. 18A-C and from the above
18 discussion that there is some overlap between nipples (and
19 Infra-mammary ridge) and tumors and also between ribs (and
20 costo-chondral junction) and tumors. Where ambiguity does
21 exist (i.e., in the relatively small overlap areas shown in
22 Fig. 18C) the distinction can generally be made based on the
23 anatomy of the portion of the patient being imaged. Thus, an
24 ambiguous tumor/nipple far from the nipple would be
25 classified as a tumor and a tumor/rib far from the ribs would
26 be classified as a tumor. Where the anatomy does not allow
27 for a clear determination, such as for example a tumor which
28 is close to the nipple, an additional view and/or a different
29 breast position, palpation or other methods of separating the
30 anomaly from the normal tissue will generally remove the
31 ambiguity.
32 While a particular impedance imaging system has been
33 described as the basis for determining the type of tissue
34 underlying the anomalies (and causing them) The method is
35 also believed to be generally useful in tissue type
36 determination using other types of impedance imaging systems
37 and also in situations where no image is generated.
38 For example, the method is also potentially useful to
39 determine tissue types in situations where either a single

1  impedance probe is us d or where the image is small and only
2  anomalous areas ar imaged. In these cases the comparison for
3  d termining the measures is mad betwe n the values of
4  capacitanc or conductanc measured for th anomalous region
5  as compared to the capacitance or conductance measured for a
6  nearby region known to be normal.
7      The method is also useful for determining the type of
8  tissue which is pierced by a biopsy needle or contacted
9  directly by a probe such as the finger probe of Fig. 7A of
10 the invasive probes of Figs. 8-10. In these cases a
11 comparison may be made between values at the tissue to be
12 characterized and other "normal" tissue.
13     Figs. 17A and 17B show a block diagram of a preferred
14 embodiment of a system 200 which incorporates a number of
15 multi-element probes. It should be understood that the exact
16 design of system for impedance imaging will depend on the
17 types of probes attached to the system and the exact imaging
18 modalities (as described above) which are used.
19     As shown in Figs. 17A and 17B the preferred system can
20 incorporate biopsy needle probe 154, two plate probes 28, 30
21 such as those shown in Figs. 1-3, scan zoom probe 100 such as
22 that shown in Fig. 6A, conformal probe 139 such as that shown
23 in Fig. 7B, a bra-cup probe, finger/glove probe 130 such as
24 that shown in Fig. 7A, laparoscopic probe 150 such as that
25 shown in Fig. 9 or an intra-operative probe 140 as shown in
26 Fig. 8. Furthermore, when three probes are used as in Fig.
27 11E, provision is made for attachment of a third plate probe.
28 The position of the plate and needle probes is controlled by
29 controller 181 as described in respect to Fig. 11D.
30     The probes as connected via a series of connectors,
31 indicated by reference numeral 302 to a selection switch 304
32 which chooses one or more of the probes in response to a
33 command from a DSP processor 306. Selection switch 304
34 switches the outputs of the probes, namely the signals
35 detected at the sensing elements of the probes (or amplified
36 versions of these signals) to a set of 64 amplifiers 308, one
37 amplifier being provided for each sensing element. For those
38 probes, such as the large plate probes, which have more than
39 64 sensing elements, the selection switch will (1)

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1 sequentially switch groups of 64 sensing elements to
2 amplifier set 308, (2) choose a subset of sensing elements on
3 a coarser grid than the actual array by skipping some
4 elements, as for example every second element, (3) sum
5 signals from adjacent elements to give a new element array of
6 lower resolution and/or (4) choose only a portion of the
7 probe for measurement or viewing. All of these switching
8 activities and decisions are communicated to the switch by
9 DSP processor 306 which acts on command from a CPU 312. The
10 output of the amplifiers is passed to a multiplexer 307 where
11 the signals are serialized prior to conversion to digital
12 form by a, preferably 12-bit, A/D convertor 310. A
13 programmable gain amplifier 309, preferably providing a gain
14 which is dependent on the amplitude of the signals, is
15 optionally provided to match the signal to the range of the
16 A/D convertor. The output of A/D 310 is sent to the DSP for
17 processing as described above. In a preferred embodiment of
18 the invention DSP 306 is based on a Motorola MC 68332
19 microprocessor.
20      While 64 amplifiers has been chosen for convenience and
21 lower cost, any number of amplifiers can be used.
22      The DSP calculates the impedance results and send the
23 results to CPU 312 for display on a graphic data display 16,
24 printing on a printer 18 or other output signals generation
25 as described above by a light indicator 314 or a sound
26 indicator 316.
27      Alternatively, the DSP directs signal sampling and
28 averages together the samples or pre-processes them, sending
29 the averaged or pre-processed samples to CPU 312, which then
30 performs the impedance calculations.
31      The CPU may also receive images from video camera 256,
32 for example, when used with an intra-operative probe, from an
33 endoscopic optics and camera system 320, for example when
34 the camera views the outer surface of the laparoscopic probe
35 or from an ultra sound imager 322, for example, in biopsy
36 performance as shown in Figs. 11A and 11B. When an image is
37 acquired from one of these cameras a frame grabber 324 is
38 preferably provided for buffering the camera from the CPU. As
39 described above, the CPU combines these images with the

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1 impedance images provided by one or more probes for display
2 or other indication to the operator.
3       Fig. 15 also shows a programmable reference signal
4 generator 326 which receives control and timing signals from
5 the DSP. The reference signal generator generates excitation
6 signals which are generally supplied, during impedance
7 imaging, to reference probe 13, which, as described above, is
8 placed at a point (or at more than one point) on the body
9 remote from the region of impedance measurement. Signal
10 generator 312 may produce a sinusoidal waveform, pulses or
11 spikes of various shapes (including a bipolar square shape)
12 or complex polychromic waveforms combining desired excitation
13 frequencies. Appropriate impedance calculations, in DSP 306
14 or in CPU 312, are implemented in accordance with the
15 waveform of the excitation.
16       Where a breast is imaged and one of the two plates is
17 used as the source of excitation, as described above, the
18 output of signal generator is sent to the exciting plate
19 (signal paths not shown for simplicity). A current overload
20 sensor 330 is preferably provided after the signal generator
21 to avoid overloads caused by short circuits between the
22 reference probe and the imaging probe or ground.
23       Also shown on Fig. 17A is an internal calibration
24 reference 332 which is preferably used for internal
25 calibration of the system and for testing and calibration of
26 the probes.
27       For internal testing and calibration, calibration
28 reference 232 receives the signals generated by the
29 programmable reference signals generator as passed to the
30 selection switch, in series with an internal admittance in
31 the calibration reference, as selected by the DSP processor.
32 The DSP processor computes the admittance from signals
33 received from the A/D convertor and compares the computed
34 admittance with the actual admittance provided by internal
35 calibration reference 332. This comparison can be provide an
36 indication that the system requires adjustment or repair or
37 can be used to calibrate the system.
38       Similarly, the output of calibration reference 332 may
39 be provided to probe cover 88 for calibration and quality

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1  assurance of a plate or scan probe as described above. Under
2  this situation, the DSP instructs selection switch 304 to
3  choose the input from the respective probe.
4      Also provided is a user interface 334 such as a
5  keyboard, mouse, joystick or combinations thereof, to allow
6  the operator to enter positional information via the screen
7  and to choose from among the probes provided and from the
8  many options of calculation, display, etc.
9      Although described together as the preferred embodiment
10 of the invention, it is not necessary to use the probes of
11 the invention, the methods of calculation of impedance and
12 impedance characteristics of the invention and the preferred
13 apparatus of the invention together. While it is presently
14 preferred that they be used together they may each be used
15 with probes, calculation methods and apparatus for impedance
16 imaging as applicable and as available.
17     Certain aspects of the invention have been described
18 with respect to a biopsy needle or with respect to placement
19 of such a needle. It should be understood that such
20 description and aspects of the invention are equally
21 applicable to positioning needles, catheters, endoscopes,
22 etc.
23     Although various embodiments, forms and modifications
24 have been shown, described and illustrated above in some
25 detail in accordance with the invention, it will be
26 understood that the descriptions and illustrations are by way
27 of example, and that the invention is not limited thereto but
28 encompasses all variations, combinations and alternatives
29 falling within the scope of the claims which follow:
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